

FIG._1A

- 1 GCTGGGCTAA ACTGGGCTAG CCTGAGCTGG GCTGAACTGG GCTGCTGGGC
- 51 TGGACTGGGT AAGCTGGGCT GAGCTGGGTT GGGTGGAAAT GGGCTGAGCT

FIG._2B

- 1 GGTTTGGCTG GGCTGGGCTG GGCTGGGCTG GGTTCAGCTG AGCGGGTTGG
- 51 GTTAGACTGG GTCAAACTGG TTCAGC

FIG._2C

GERMLINE & LOCUS

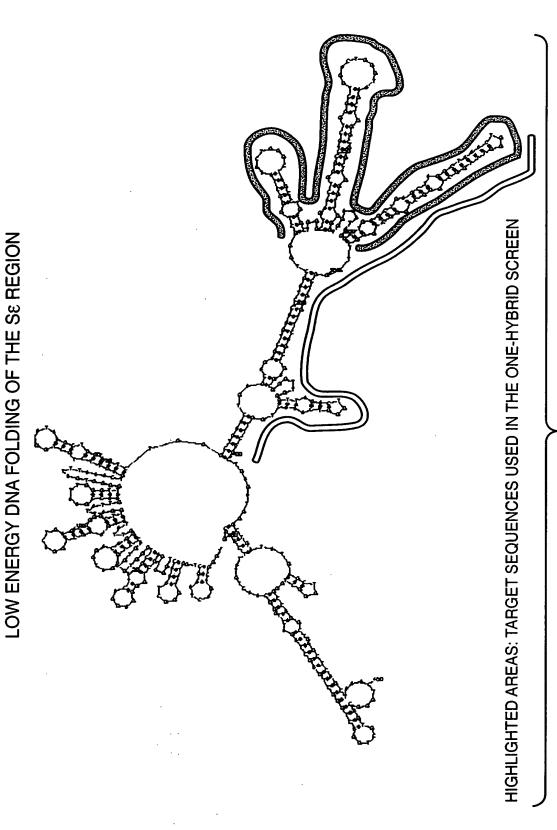
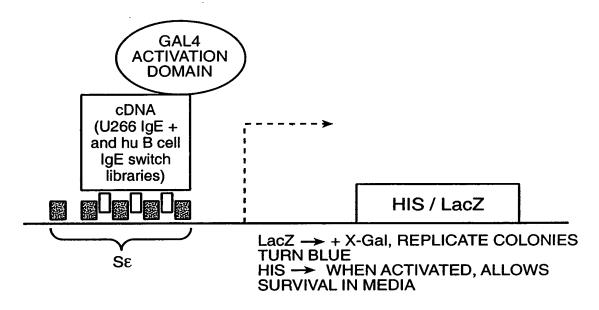
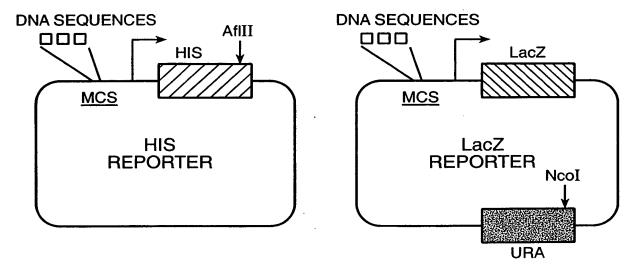


FIG._2A

YEAST ONE-HYBRID SCREENING





ONE HYBRID REPORTER VECTORS

DNA SEQUENCES OF INTEREST ARE INSERTED INTO THE MULTIPLE CLONING SITES (MCS). THE ENZYME USED TO LINEARIZE THE VECTOR IS SHOWN WITH A SOLID ARROW. DASHED ARROWS INDICATE THE TRANSCRIPTION OF THE REPORTER GENE.

DND39 + IL-4

DND39 - IL-4

MC-116 + IL-4

MC-116 - IL-4

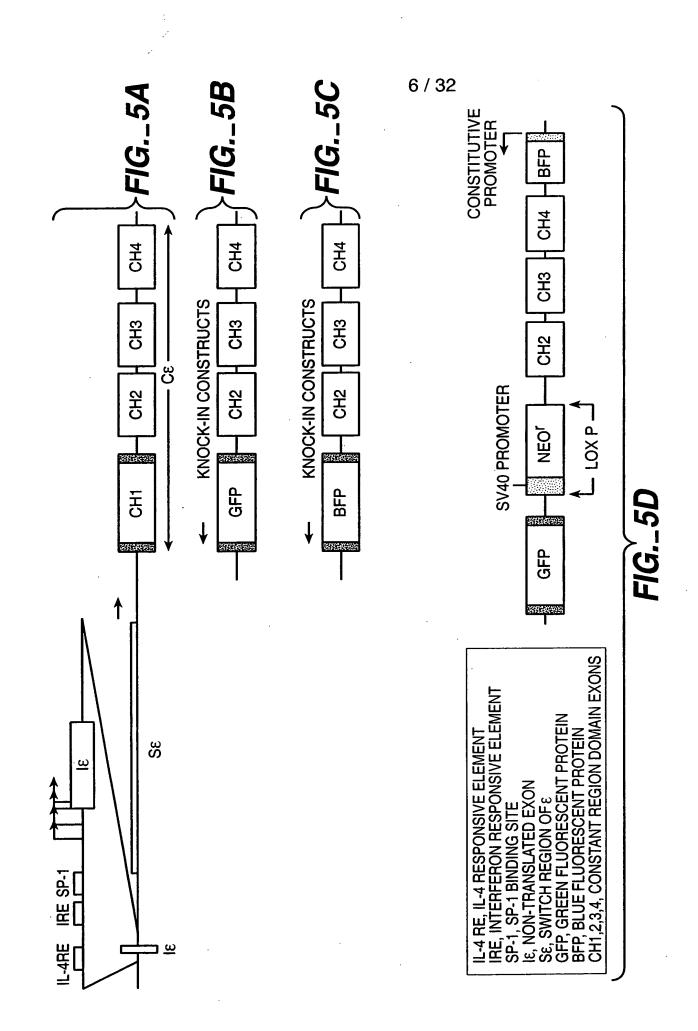
CA-46 + IL-4

CA-46 - IL-4

NEG. CONT.

246bp

FIG._4



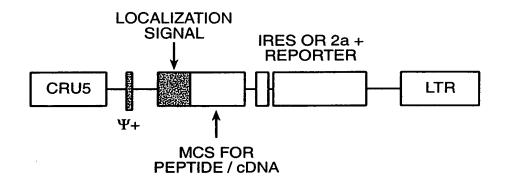


FIG._6

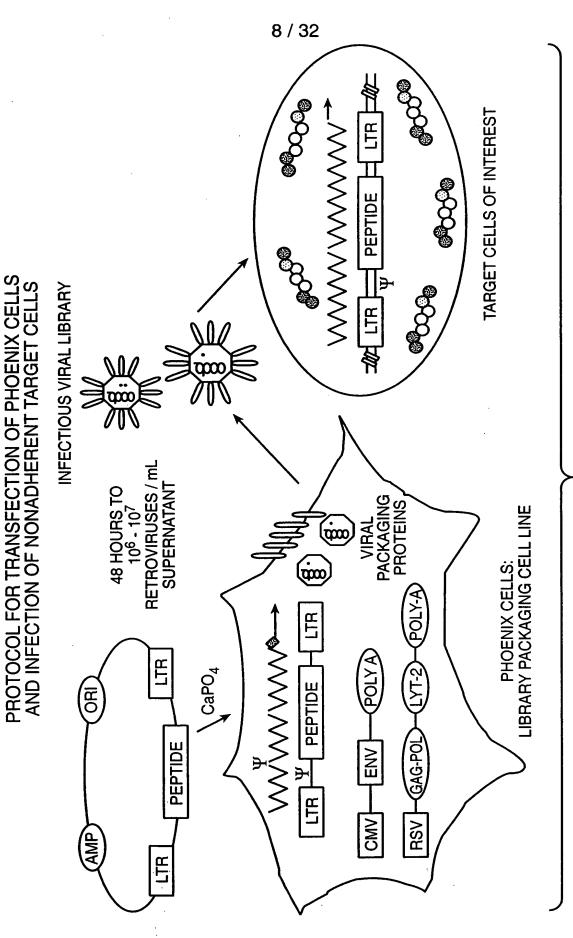
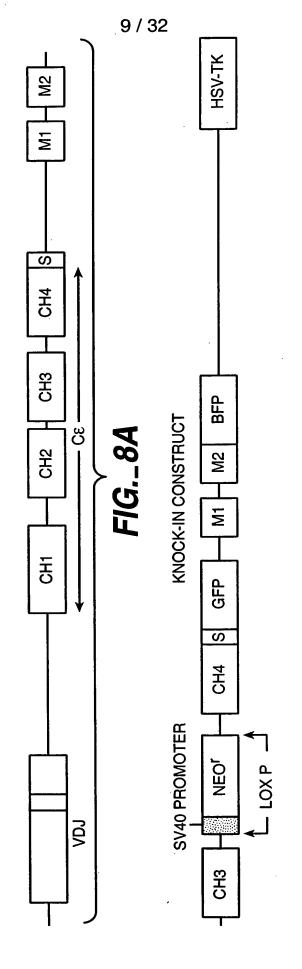


FIG._7

ε HEAVY CHAIN GFP / BFP KNOCK-IN CELL LINE

U266 ε HEAVY CHAIN



UZ66 CELLS ARE TRANSFECTED AND SELECTED WITH G418. SURVIVORS ARE TREATED WITH GANCICLOVIR (HSV-TK DELETED DURING HOMOLOGOUS RECOMBINATION). RT-PCR IS PERFORMED TO CONFIRM HOMOLOGOUS RECOMBINATION. THOSE CLONES ARE TRANSFECTED WITH crop to remove the SV40 neomycin resistance gene.

FIG._8B

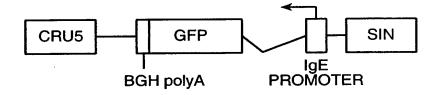


FIG._9A

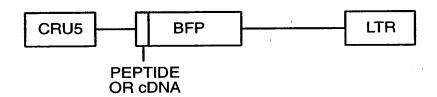
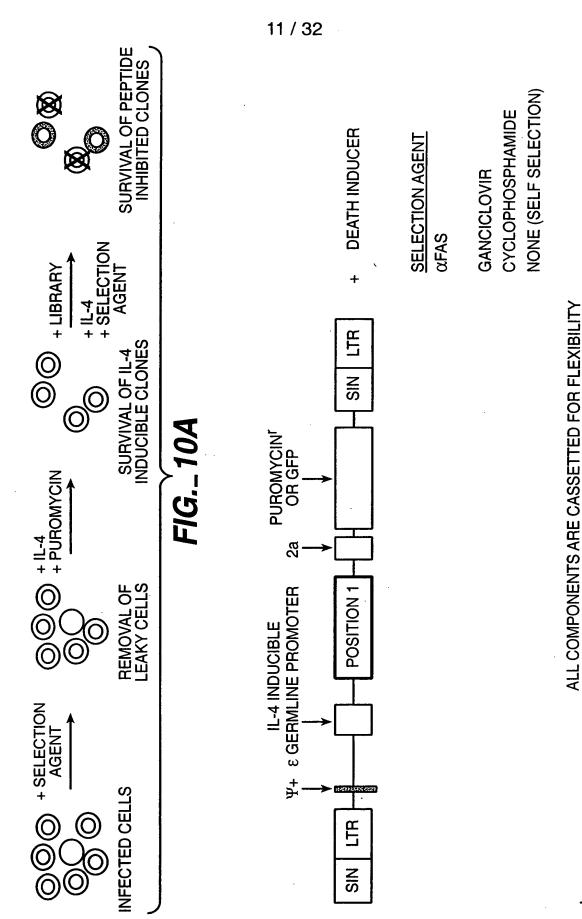


FIG._9B



1-845 CMV promoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended Ψ region
2146-2173 two Bstx1 peptide cloning sites
2205-2723 ECMV IRES (cloned as EcoR1/Msc1 fragment from pCITE-4a [Novagen])
2746-3465 GFP coding region
3522-4115 3' LTR
4122-6210 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATCC CAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATCAA TTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAA **ATGGCCCGCCTGGCTGACCGCCCAACGACCCCCCCCCCATTGACGTCAATAATGACGTATG** TTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGT ${f a}{f a}{f A}{f C}{f T}{f G}{f C}{f C}{f A}{f G}{f T}{f A}{f C}{f A}{f G}{f T}{f A}{f T}{f A}{f C}{f C}{f C}{f C}{f C}{f C}{f C}{f T}{f A}{f T}{f G}{f C}{f G}$ TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTC CTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGC **AGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCA** TTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGAGGTCTATATAA GCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACT GAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGT CTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTT CATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACCACCGACCCACCACCG GGAGGTAAGCTGGCCAGCAACTTATCTGTGTCTGTCCGATTGTCTAGTGTCTATGACTGA TTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTATCTGGCGGACCCGTGG TGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAGACGTCCCAGGGACTTCGG GGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATCGTTTTGGACTCTTTGGTG CACCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGACGAGAACCTAAAACAGTTCC GCTGCAGCATCGTTCTGTGTTGTCTGTCTGACTGTGTTTCTGTATTTGTCTGAAAAATA TCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTGACCTTAGGTCACTGGAAAGATG TCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAAGAAGAGACGTTGGGTTACCTTCT GCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGCCGCGAGACGGCACCTTTAACCGAG **ACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCACCTGGCCCGCATGGACACCCAGACC** CCTTTGTACACCCTAAGCCTCCGCCTCCTCTTCCTCCATCCGCCCCGTCTCTCCCCCTTG **AACCTCCTCGTTCGACCCCGCCTCGATCCTCCCTTTATCCAGCCCTCACTCCTTCTCTAG** GCGCCCCATATGGCCATATGAGATCTTATATGGGGCACCCCCGCCCCTTGTAAACTTCC CTGACCCTGACATGACAAGAGTTACTAACAGCCCCTCTCTCCAAGCTCACTTACAGGCTC TCTACTTAGTCCAGCACGAAGTCTGGAGACCTCTGGCGGCAGCCTACCAAGAACAACTGG ACCGACCGGTGGTACCTCACCCTTACCGAGTCGGCGACACAGTGTGGGTCCGCCGACACC AGACTAAGAACCTAGAACCTCGCTGGAAAGGACCTTACACAGTCCTGCTGACCACCCCCA CCGCCCTCAAAGTAGACGGCATCGCGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGA CCCCGGGGGTGGACCATCCTCTAGACTGCCGGATCTCGAGGGATCCACCACCATGGACCC GGTTATTTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTG TCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGT CGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGC CACGTGTATAAGATACACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGTTGGA TAGTTGTGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATG CCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACAT GTGTTTAGTCGAGGTTAAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTGGTTTTCCT TTGAAAAACACGATGATAATATGGGGGATCCACCGGTCGCCACCATGGTGAGCAAGGGCG AGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCC ACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGA AGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGA CCTACGGCGTGCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCA ${ t A}{ t G}{ t T}{ t C}{ t C}{ t C}{ t C}{ t A}{ t A}{ t G}{ t C}{ t C}{ t C}{ t A}{ t C}{ t C}{ t C}{ t C}{ t A}{ t C}{ t C}{ t C}{ t A}{ t C}{ t C}{ t C}{ t A}{ t C}{ t C}{ t C}{ t A}{ t C}{ t C}{ t C}{ t A}{ t C}{ t C}{ t A}{ t C}{ t C}{ t C}{ t A}{ t C}{ t$ <u>ACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGC</u> TGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACT ACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACT TCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGA ACACCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGT CCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGA CCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAAAGCGGCCGCTCGACGA TARARTRARAGATTTTATTTAGTCTCCAGAARAAGGGGGGAATGAAAGACCCCACCTGTA GGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGA GAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACA GGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTG **AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAA** CAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTC CAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCG CTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCC TCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAA ACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGA GTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGG GAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTCACATGCAGCATGTAT CAAAATTAATTTGGTTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAAT GAATCGGCCAACGCGCGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCT GGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGG CCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCG CCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGG ${ t ACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGAC$ CCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA TAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGT GCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG **AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACAC**

TAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGT **GCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTCTACGGG** GTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAA TATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTC **AGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC** GATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC **ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCCGAGCGCAGAAGTGG** TCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAG TAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCCATTGCTACAGGCATCGTGGTGTC **ACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTAC ATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAG AAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC** TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTG **AGANTAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAACACGGGATAATACCGC** GCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACT CTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTG **ATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAA TCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATG** TATTTAGAAAATAAACAAATAGGGGTTCCGCGCACATTTC

FIG._11A-3

1-845 CMVpormoter/R/U5 5' LTR

1322 GAG ATG-ATC mutation

850-2100 extended region

2151-2865 GFP coding region

2866-2894 GGGSGGG linker

2895-2952 FMDV 2a cleavage sequence

2953-3004 Bstx1/Bstx1/HinD3/Hpa1/Sal1/Not1 polylinker

3052-3645 3' LTR

3652-5715 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC **AATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGG TATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTT ACGGTAAACTGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTA** TTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGG GACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTC t CCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCA**AAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCATGTACGGTGGGA** GGTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCCAGTC CTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCA TCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGT CAGCGGGGTCTTTCATTTGGGGGCTCGTCCGGGATCGGGAGACCCCTGCCCAGGGACC TAGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGT **ATCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCGGCCGCAACCCTGGGAG ACGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGAT** CGTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGA CGAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAA TTTCTGTATTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTT GACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCA **AGAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGG** CCGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTC **ACCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGG** CTTTTGACCCCCCTCCCTGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCTTT CCTCCATCCGCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCGCCTCGATCCTC CCTTTATCCAGCCCTCACTCCTTCTCTAGGCCGCCCCCATATGGCCATATGAGATCTTAT **ATGGGGCACCCCGCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAAC AGCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAG** GAGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGG **AAAGGACCTTACACAGTCCTGCTGACCACCCCCCACCGCCCTCAAAGTAGACGGCATCGC** ${f AGCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTA}$ GACTGCCGGATCTCGAGGGATCCACCATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGG

GTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTC CGGCGAGGGCGAGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCA CCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAG TGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCC CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCC GCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATC GACTTCAAGGAGGACGGCAACATCCTGGGGCACAAGCTGGAGTACAACTACAACAGCCA CAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTCAAGATCC GCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAACACCCCCC ${ t A}$ TCGGCGACGGCCCCGTGCTGCCCGACAACCACTACCTGAGCACCAGTCCGCCCT GAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCG CCGGGATCACTCTCGGCATGGACGAGCTGTACAAGGAATTCGGAGGTGGCAGCGGTGGC GGTCAGCTGTTGAATTTTGACCTTCTTAAACTTGCGGGAGACGTCGAGTCCAACCCTGG GCCCACCACCACGATGGAAGCTTCCATTAAATTGGTTAACGTCGACGCGGCCGCTCGAC GATAAAATAAAAGATTTTATTTAGTCTCCAGAAAAAGGGGGGGAATGAAAGACCCCACCT GTAGGTTTGGCAAGCTAGCTTAAGTAACGCCATTTTGCAAGGCATGGAAAAATACATAA CTGAGAATAGAGAAGTTCAGATCAAGGTCAGGAACAGATGGAACAGCTGAATATGGGCC AAACAGGATATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGAA CAGCTGAATATGGGCCAAACAGG&TATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGG CCAAGAACAGATGGTCCCCAGATGCGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCA GATGTTTCCAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCA ATCAGTTCGCTTCTCGCTTCTGTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGC CCACAACCCCTCACTCGGGGCGCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGT GTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAG GGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGT CTCGCTGCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTCAGCGGGGTCTTCA CATGCAGCATGTATCAAAATTAATTTGGTTTTTTTTTCTTAAGTATTTACATTAAATGGC CATAGTTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCT CTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTA TCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAA GAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG **CGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG** AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCT CGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCCTT CGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT **ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAG** CAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTG AAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCT CAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACG TTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATT AAAAATGAAGTTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCAT ${f A}$ GTTGCCTG ${f A}$ CTCCCGTCGTGT ${f A}$ GAT ${f A}$ ACT ${f A}$ CGGGAGGGCTT ${f A}$ CCATCTGGCC CCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATA FIG._11B-3

1-845 CMVpormoter/R/U5 5' LTR
1322 GAG ATG-ATC mutation
850-2100 extended region
2146-2173 two Bstx1 peptide cloning sites
2173-2214 EoR1/Apa1/Hpa1/Not1 polylinker
2262-2855 3' LTR
2855-4901 pGEM backbone (pUC origin, ampR)

ATCACGAGGCCCTTTCGTCTTCAAGAACAGCTTTGCTCTTAGGAGTTTCCTAATACATC CCAAACTCAAATATATAAAGCATTTGACTTGTTCTATGCCCTAGTTATTAATAGTAATC AATTACGGGGTCATTAGTTCATAGCCATATATGGAGTTCCGCGTTACATAACTTACGGT ${f AAA}$ TGGCCCGCCTGGCTGACCGCCCAACGACCCCCCCCCCATTGACGTCAATAATGACGT $oldsymbol{\mathtt{A}}$ TGTTCCC $oldsymbol{\mathtt{C}}$ ATAGGGACTTTCCATTGACGTC $oldsymbol{\mathtt{A}}$ ATGTTT $oldsymbol{\mathtt{A}}$ CGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTAT TGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG **ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGG** TTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCT CCACCCCATTGACGTCAATGGGAGTTTGTTTTTGGCACCAAAATCAACGGGACTTTCCAA ${ t A}{ t A}{ t T}{ t G}{ t T}{ t G}{ t A}{ t C}{ t A}{ t A}{ t C}{ t T}{ t C}{ t C}{ t C}{ t C}{ t C}{ t A}{ t T}{ t G}{ t A}{ t C}{ t G}{ t C}{ t G}{ t A}{ t A}{ t T}{ t G}{ t G}{ t C}{ t G}{ t G}{ t C}{ t G}{ t A}{ t A}{ t T}{ t G}{ t G}{ t C}{ t G}{ t G}{ t C}{ t G}{ t A}{ t A}{ t T}{ t G}{ t G}{ t C}{ t G}{ t G}{ t C}{ t G}{ t A}{ t A}{ t T}{ t G}{ t G}{ t C}{ t G}{ t C}{ t G}{ t A}{ t A}{ t C}{ t G}{ t$ GTCTATATAAGCAGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCCAGTCC TCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGTTGCAT CCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTACCCGTC ${ t A}$ GCGGGGGTCTTTC ${ t A}$ TTTGGGGGCTCGTCCGGG ${ t A}$ TCGGGAGACCCCTGCCCAGGGACCA AGTGTCTATGACTGATTTTATGCGCCTGCGTCGGTACTAGTTAGCTAACTAGCTCTGTA TCTGGCGGACCCGTGGTGGAACTGACGAGTTCGGAACACCCCGGCCGCAACCCTGGGAGA CGTCCCAGGGACTTCGGGGGCCGTTTTTGTGGCCCGACCTGAGTCCAAAAATCCCGATC GTTTTGGACTCTTTGGTGCACCCCCCTTAGAGGAGGGATATGTGGTTCTGGTAGGAGAC GAGAACCTAAAACAGTTCCCGCCTCCGTCTGAATTTTTGCTTTCGGTTTGGGACCGAAG TTCTGT&TTTGTCTGAAAATATCGGCCCGGGCCAGACTGTTACCACTCCCTTAAGTTTG ACCTTAGGTCACTGGAAAGATGTCGAGCGGATCGCTCACAACCAGTCGGTAGATGTCAA GAAGAGACGTTGGGTTACCTTCTGCTCTGCAGAATGGCCAACCTTTAACGTCGGATGGC CGCGAGACGGCACCTTTAACCGAGACCTCATCACCCAGGTTAAGATCAAGGTCTTTTCA CCTGGCCCGCATGGACACCCAGACCAGGTCCCCTACATCGTGACCTGGGAAGCCTTGGC TTTTGACCCCCCCCCCGGGTCAAGCCCTTTGTACACCCTAAGCCTCCGCCTCCTCTTC CTCCATCCGCCCCGTCTCTCCCCCTTGAACCTCCTCGTTCGACCCCCGCCTCGATCCTCC CTTTATCCAGCCCTCACTCCTTCTCTAGGCGCCCCCATATGGCCATATGAGATCTTATA TGGGGCACCCCCGCCCCTTGTAAACTTCCCTGACCCTGACATGACAAGAGTTACTAACA GCCCCTCTCTCCAAGCTCACTTACAGGCTCTCTACTTAGTCCAGCACGAAGTCTGGAGA CCTCTGGCGGCAGCCTACCAAGAACAACTGGACCGACCGGTGGTACCTCACCCTTACCG **AGTCGGCGACACAGTGTGGGTCCGCCGACACCAGACTAAGAACCTAGAACCTCGCTGGA** AAGGACCTTACACAGTCCTGCTGACCACCCCCACCGCCCTCAAAGTAGACGGCATCGCA GCTTGGATACACGCCGCCCACGTGAAGGCTGCCGACCCCGGGGGTGGACCATCCTCTAG ACTGCCGGATCTCGAGGGATCCACCACCATGGACCCCCATTAAATTGGAATTCGGGGCC TAACGCCATTTTGCAAGGCATGGAAAAATACATAACTGAGAATAGAGAAGTTCAGATCA

AGGTCAGGAACAGATGGAACAGCTGAATATGGGCCAAACAGGATATCTGTGGTAAGCAG TTCCTGCCCGGCTCAGGGCCAAGAACAGATGGAACAGCTGAATATGGGCCAAACAGGA TATCTGTGGTAAGCAGTTCCTGCCCCGGCTCAGGGCCAAGAACAGATGGTCCCCAGATG CGGTCCAGCCCTCAGCAGTTTCTAGAGAACCATCAGATGTTTCCAGGGTGCCCCAAGGA CCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTCGCTTCTCGCTTCTGTT CGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCCACAACCCCTCACTCGGGGCGCC **AGTCCTCCGATTGACTGAGTCGCCCGGGTACCCGTGTATCCAATAAACCCTCTTGCAGT** TGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGACTAC CCGTCAGCGGGGGTCTTTCATTTCCGACTTGTGGTCTCGCTGCCTTGGGAGGGTCTCCT CTGAGTGATTGACTACCCGTCAGCGGGGTCTTCACATGCAGCATGTATCAAAATTAAT TTGGTTTTTTTTCTTAAGTATTTACATTAAATGGCCATAGTTGCATTAATGAATCGGCC **AACGCGCGGGGAGAGGCGGTTTGCGTATTGGCGCTCTTCCGCTTCCTCGCTCACTGACT** CGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCA <u>AAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCC</u> CTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTA TAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCT GCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATA GCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTG CACGAACCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC ${ t CAACCGGTAAGACACGACTTATCGCCACTGGCAGCCACTGGTAACAGGATTAGCA}$ GAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC <u>ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAG</u> <u>AGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTT</u> GCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCT ${f A}{f C}{f G}{f G}{f G}{f T}{f C}{f A}{f C}{f A}{f C}{f A}{f A}{f A}{f A}{f C}{f T}{f C}{f A}{f C}{f G}{f T}{f T}{f A}{f G}{f G}{f A}{f T}{f T}{f T}{f G}{f G}{f A}{f T}{f T}$ ATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTGCGCAAATCAA TCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCA CCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTA GATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAG CGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGA **AGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAG** TCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCC TCCGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCAC TGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTAC TCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC **AACACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAAC GTTCTTCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAA** CCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCACCAGCGTTTCTGGGTG **AGCAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTT** GAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTC ATGACATTAACCTATAAAAATAGGCGT

FIG._11C-2

gcaaacaacagtiggctiggctacaagtiggsggctiggctiggctiggcaaacctacaggtigggggtctitcaticcc $|ersigma||G_n$, ||Z|A|

TGCTATTGTCTTCCCAATCCTCCCCCTTGCTGTCCTGCCCCACCCCCCCAGAATAGAATGACACCTACTCAGACA

atcacgaggccctttcgtcttcaagaacagctttgctcttaggagtttcctaatacatccaaaccccaaactccaaatatataaagc atttgacttgttctatgccctagttattaatagtaatcaattecgggggtcattagttcattcatagcccatatatggagttccg ttoccatagtaacgccaatagggactttocattgacgtcaatgggtggagtagtacttaagggtaaactgcccacttggcagta catcaagtgtatcatatgccaagtacgccccctattgacgtcaatgacggtaaatgacggtaaatggcccgcctggcattatgcccagta catgacettatgggactttcctacttggcagtacatctacgacatetatggtcatcgctattaccatgggtgatgcggtttttggc agtacatcaatgggcgtggatagcggtttgactcacgggggatttccaaggtctccaaccccattgacgtcaatgggagtttg teteetetgagtgattgaetaeeegteageggggtettteatttgggggeteggeggategggateggggateggggaggaggag ggaccaccaccaccaccagggaggtaagctggccagcaacttatctgtgtctggtcgattgtctgatcta tgtetetgtetgaetgtgtttetgtatttgtetgaaaaatatgggeeegggeeagaetgttaecaeteettaagtttaag としたしな好であてのあるねもてのななななしししてのなるなもないしながあるのであることのでこののとしなるのののあるとならないののであるののであるののであるののである。 acggtgggaggtctatatatagagcagagctcaataaaagagcccaacaacccctcactcggggcgccagtcctccgattgact ttttatgegeetgegtegtaetagttagetaactagetetagetetgtatetggeggaeeegtggtggaactgaegagtteggaa こゑでこで努好でこ好こぉゑでこことの女女をななこのでこのなななななななななななこのでしてしているののここのないのでなるない。 tegttttggactetttggtgcacccccttagaggagggatatgtggtttctggtaggagagaggagaacctaaaaacagttcc gctctgcagaatggccaacctttaacgtcggatggccgcgagacggcacctttaaccgagacctcacccaggtttaag atcaaggtetttteacetggeeeggaeatggaeaceeagaeeaggteeetaeategtgaeetgggaageettggetttga ccccctccctgggtcaagccctttgtacaccctaagcctccgcctcctcctcctccatccgcccggcccgtctc aacctectegttegaeceegeetegateetectetttateeageeeteactettetetetggegegeeeeatatggeeatat accgaccggtggtacctcacccttaccgagtcggcgacacagtgtggggtccggccgacaccagactcagacttagaacct CGCCCaCGtgaaggctgccgaccccggggggtggaccatctctagactgccGGATCTCGAGGATCCTCCTCCAGCATGCA

ccaagetttggatttcatttctgaagttttgaattttctgagtcactagtaatgtccttgaggatgatgatagtctttc ccaattacgaagcagttgaactttctgttctgtctgtgtgtcttggacattgtcattcttgatctcatctattttggcttcat tgacaccattettegaacaaageetttaaettgaettagtgteatgaeteeaggaatteggtggtggtgatatttaeteaag tcaacatcagataaatttattgccactgtttcaggatttaaggtttggagattcaggagttggagattcatgagaaccttggttttcctgtg cttctgcatgttttctgtacttcctttctctccaccaaacaattagtggaattggcaaaagaagaagaagacaaac CCAACCGGTTTCTGGGACTTTCTTGCTGCTTTTGTATTGCTGGTTGCTGTGCATGGCTCAAGGGTTCCATGTTCACAC gaggcgcagcgaacacagtgttcacagccaggagaatcgcagtagaagtctggtttgcacttgcacttggtattctggg **CAGGGTGCAGTTTGTTTCCACTTCTAAACCATGCTCTTCATCGCAGAGTGTGCCATCTTCTGCATTTATCAGCATAATGGT** TTTTTACCAGGTTGGCATGGTTGACAGCAAAATGGGCCTCCTTGATAAATCCTTCTGAGCAGTTTTTATCAGTTTTCATG

aaatcacgccatgtagtgtattgaccgattccttgcggtccgaatgggccgaacccgctcggtctggctaagatcggccgc agcgatcgcatccatggcctccgcgaccggctgcagaacaggagcgggcagtttcggttcagggcaggtcttgaaacgtgacac cctgtgcacggcgggagatgcaataggtcaggctctcgctaaattccccaatgtcaaggaactccggaagtgcg ccetcctacategaagetgaaageaegagattettegeeeteegagagetgeateaggteggagaegetgtegaaetttt cgatcagaaacttctcgacagacgtcgcggtgagttcagggcttttttcatggtattatcatcgtgtttttttcaaaggaaaac cacgteceegtggtteegggggeettagaegttttttaaeettegaetaaaeatataaageatgtaaageatgtgeaegaggeeeeag atcagatcccatacaatggggtaccttctggggcatccttcagccccttgttgaatacgcttgaggagagccatttgactc tttecascaactatecaascteacaacgtggeactggggtttgtgecgeetttgeaggtgtatettataeaegtggettttgg gacgagtgctgggggcgtcggtttccactatcggcgagtacttctacagccatcggtcaggtccagggccagg caagoteeggatgeeteegetegaagtagegeetegetgetgeteeataeaageeaaggeeteeaggaagaagaagatgttg gegaeetegtattgggaateeegaaeategeetegeteeagteaatgaeeggetgateatgeggeeattgteegteaggae cctgcgcgacgcactgacggtgtcgtccatcacagtttgccagtgacacatggggatcacatgggggatcagcaatcgcgcatatg gecgatgeaaagtgeegataaacataacgatettegtagaaaceateggegegegeagetatttaceegeaggaeatateeaeg

CCCTTTTTCTGGAGACTAAATAAATCTTTTATTTTAtcgatagatcccggtcggcatctactctattcctttgccctcg

gregceaaaccceacaegeactataaagataccagecettecccctegaagctcctctcgegegectctctgtccgaccc $F \| G_{n-1} \| 2 G$ **ATGGAACAGGCAATAAAAGAGCCCACACCCCTCACTCGGGGCGCCCAGTCCTCCGATTGACTGAGTCGCCCGGGTACCCG** CTACCCGTCAGCGGGGTCTTTCAcatgcaGCATGTATCAAAATTAATTTGGTTTTTTTTTTTTAAGTATTTACATTAAAT TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGGGGAGAGGGCGGTTTGCGTATTGGGCG taatacggttatccacagaatcaggggataacgcaggaaaagaacatgtgtgagcaaaaggccagcaaaaaggccaggaaccgt <u>aaaaaggccgcgttgctggcgtttttccataggctccgccccctgacgaggatcacaaaaaatcgacgctcaagtcagag</u> cgcactgaggtgaactggccctcggggGcgcgtgtcccagatgtgtgtgtgcagggcctcctgatggccgcagcctcctc ctgtgacccgcttggagctggcacctgagtggtggcctcacCTTGTACTCACTCCAGGTCACTGCtcgacGCGGCC **GCTCGAcgataaaaaaaaaaattttatttactccagaaaaaagggggaatgaaagaccccacctgtaggtttggcaag** TGTATCCAATAAACCCTCTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGGAGGGTCTCCTCTGAGTGATTGA **CCAGAGGCAGGACAGCCCCAGATCCACACCATGGTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAGA** aaacgcaagagtcttctctctcgacaagcccagtttctattggtctccttaaacctgtcttgtaactttac CTGCCCAGTGCCTCACGACCAACTTctgcaggaattcctggacagctcccagatgatcagtaaccgtggttgttatttct gtgccgggcagtggagcctgggtagggggggctctgcctcagtgctttcagctaaggggctaaaaatgggggtgggaacccCaggaagg cccgggccgccctggaagttcccttttctctctctgttcttgggaagtcgattgagcaacagcgggggtcaggttgaggctcc ttcäctaccgatgcacacaccgagtgctGgggggaggttctctctctctcagggcccaaacCccagggccccagggtcctgcctaggtccc

cagggttattgtctcatgacattaacctataaaaataggcgt

TGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTC TAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAG TTABARTTABABATGAAGTTTGCGCAAATCAATCTAAAGTATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAAT CAGTGAGGCACCTATCTCAGGGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCGTCGTGTAGATAACTACGA TACGGGAGGGCTTACCATCTGGCCCCCAGTGCTGCAATGATACCGCGAGACCCCACGCTCACCGGCTCCAGATTTATCAGCA CCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGCCATTGCTACAGGCATCGTGGTGTCAC GCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCCATGTTGTGCAAA **ACTGCATAATTCTCTTTACTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgag** aatagtgtatgcggcgaccgagttgctcttgcccggcgtcaacacggggataatacggggcgccacatagcagaactttaaaa gtgotcatcattggaaaacgttottcgggggggggcgaaactctcaagggatcttaccgctgttgagatccagttcgatgtaacc cactegtgeacecaactgatetteageatetttaettteaceegegtttetgggtggtgageaaaaaaggaaggeaaatg **AGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTAATCCGG CGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGCCTACACTAGAAGGACAGTATTTGGTATC** TGGTTTTTTTTGCTAGCAGCAGCAGATTACGCGCAGAAAAAAGGATCTCAAGAAAAGAATCCTTTGATCTTTTTAACTGGGGGT CTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTT ccgcaaaaaagggaataagggcgacacggaaatgttgaatactcatactctttttttaatatattagaagcattta

GCAAACAAACAGATGGCTGGCAACTAGAAGGCACAGTCGAGGtCTAGCTTGCCAAACCTACAGGTGGGGTCTTTCATTCCC

tgtetetgtetgaetgtgttttetgtatttgtetgaaaaatatgggeeegggeeagaetgttaceaetcetettaagttttgae cttaggtcactggaaagatgtcgagcggatcgctcacaaccagtcggtagatgtcagaagaagaagaagagacgttgggttaccttct getetgeagaatggecaacetttaaegteggatggeegegagaeggeagaeggeacetttaaeegagaeeteaeteaggttaag atcaaggtetttteacetggeeeggaeatggaeaceeeagaeeaggteeetaeategtgaeetgggaageettggetttga ccccctccctgggtcaagccctttgtacaccctaagcctccgcctcctcttcctcccatccgccccgtctcttc aaceteetegttegaceeegeetegateeteetttateeageeeteaeteeteeteeteggegegeeeeeatatggeeatat ccaagetcaettacaggetetetagtectagtecageacgaagtetggagaeetetggageggeageetaeeaagaaeage cgetggaaaggaeettaeaagteetgetgaecaeeceeegeegeeetgaegaegeetggeateggeategeagettggataeege cgcccacgtgaaggctgccgaccccggggggtggaccatctctagactgccGGATCTCGAGGATCCTCCTCCAGCATGCC atcacgaggccctttcgtcttcaagaacagctttgctcttaggagttttcctaatacatcccaaacteccaaatatatataaagc atttgacttgttctatgccctagttattaatagtaatcaattcattacggggtcattagttcatagcccatatatggagttccg tteceatagtaaegeeaatagggaetttecattgaegtcaatgggtggtggagtatttaeggtaaetgeeeaettggeagta catcaagtgtatcatatgccaagtacgccccctattgacgtcaatgacggtaaaggcccgcctggcattatgcccagta catgacettatggggactttcctacttggcagtacatetacgtatttegge agtacatcaatgggcgtggatagcggttttgactcacgggggatttccaagtctccacccattgacgtcaatgggagtttg ttttggcaccaaaaatcaaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggtaggcatgt acggtgggaggtctatatataggcaggctcaataaaagagcccaacaacaacccctcactcggggggcgccagtcctccgattgact とったったったなみなたなねったねっこってんこもなっななななななくことにもしたしななななのにこのにってのなるなもこのなるなのでもの ggaccaccgaccaccaccagggaggtaagctggccagcaacttatctgtgtctggccgattgtctagtctaggtgtctatgactga tttatgegeetgegtegtaetagttagetaattagetaageteagetetgtatetggeggaeeegtggtggaaetgaeggtgateggaa cacccggccgcaaccctgggagacgtcccaggggacttccggggggccgttttttgtggcccgacctgagtccaaaaatcccga

aaatcacgccatgtagtgtattgaccgattccttgcggtccgaatgggccgaacccgctcggctctggctaagatcggccgc agegategeatecatggeetecgegaeeggetgeagaacaggegegggeagttegggttcaggeaggeaggtettgeaaegt cetgtgeacggegggagatgeaataggteaggetetegetaaatteeceaatgteaageaetteeggaagtgegg gccgatgcaaagtgccgataaacataacgatctttgtagaaaccatcggcgcgcagctatttacccgcaggacatatccacg ccctcctacategaagetgaaageacgagattettegeecteegagagetgeateaggteggagagaegetgtegaaettt cgateagaaacttetegaeagaegtegeggtgagtteaggettttteatgatattateategtgtttttteaaggaaaae cacgtococcgtggttcoggggggcotagacgttttttaacctogactaaacatatataaagcatgtgcaccgaggcoccag atcagatecestacaatggggtacettetggggeatectteagecettgttgaataeggettgaagaegaggegagecatttgaete tttccacaacaactaccaactcacaacgtggcactggggttgcgccgcctttgcaggtgtatcttatacacgtggcttttgg e e coagaggaa chechronda cantica a cantica a cantica a contro cantica a contro con cantica a contro con cantica a contro cant gegatttgtgtaegeeegaeagteeeggeteeggateeggateggaeegattgegtegeategaeeeggegeeeaggetgeate caageteeggatgeeteegetegaagtagegeetgettetgeteeataeaagecaaeggeeteeaggaagaagaagatgttg gogacetegtattgggaateecegaacategeetegeteeagteaatgaeeggetgttatgeggeeattggae attgttggagccgaaatccgcgtgcacgaggtgccggaacttcggggcagtcctcgggccccaaagcatcatcagcg cetgegegaeggaegeaetgaeggtgtegtecateaeagtttgeeagtgaeaeagggataeaeagggateageaateg

CCCTTTTTTCTGGAGACTAAATAAATCTTTTATTTTA togatagatecggtoggeatetetetettgcottog gacgagtgctgggggggcgtcttccactatcggcgagtacttctacaacagccatcggtccaggccaggcggcggctfctgcgg

teaacateagataaatttattgeeactgttteaggatttaaggtttggagatteatgagaacettggtttteettgt ccaattacgaagcagttgaactttctgttctgctgtgtgtcttggacattgtcattcttgactcttgatctcatctatttggcttcat tgacaccattctttcgaacaaagcctttaacttgacttagtgtcatgactccagcaatagtggtggtggtgatatttactcaag ctttctgcatgtttttctgtacttcctttctcttcacccaaacaattagtggaattggcaaagaagaagaagacaaaggccacc ccaaccggttttccggtccccttcactgagccacggggccgacaatcttctggtctctctggggctggggctgagatgtcccggtaggg tgcacaggtgagggagttcgcagcactggctttggtagtagtagttcactttctctgaaggactggcacgacagaactgaa gtacatcaccgagttgctgatgactgagcagaaatagtagccttcgttttccttgctgaacttgttcagggtgaacgt acttattattegtgtccctcatggcagaaaacagttttcgacgaattcagcttctcgcccacgttatcttgttgtgggat ggaccccaacacttcacataccaggtccaccttctgaccaagttccgg gtgeetgtggettagetteteeacteecaggataategacteaceaggata aacggtgaggccatgGTGGCTTTACCAACAGTACCGGAATGCCAAGCTTGCGGCCGCTTAAGAGCTGTAATTGAACCTGG

ccaagctttggatttcatttctgaagttttgaatttttctgagtcactagtaatgtccttgaggatgatgatgatgat tetgeaagagtaeaaagattggettttttttgagatetttaateaatgtgtgteataegettettettetteeatgaagttgatg

gagtggacacctgtggagagagaaaggcaaagtggatgtcagtaagaccaataggtgcctatcagaaacgcaagagtcttct

CTGTCTCGACAAGCCCAGTTTCTATTGGTCTCCTTAAACCTGTCTTGTAACCTTGATACTTACCTGCCCAGTGCCTCACG

CCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCACTGGTAACAGGATTAGCAGAGGGGGTATGTAGGCGGT GGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGGTCAGGGGGGGAAACCCGACAG CTTGCAGTTGCATCCGACTTGTGGTCTCGCTGTTCCTTGGAGGGTCTCCTCTGAGTGATTGACTACCGTCAGCGGGG GTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGGGAGAGAGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTTCCTCCTC gactataaagataccaggcgtttccccctggaagctccttcgtgctcctcttctcctgttccgaccctgccgcttaccg CTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGT cetetgettecaagaaaageettgtgaagaaaaggatgggggggccttttgtgcaaggagaatgaggcgcaetgaggtgaaetg gecetegggggegegegtgteceagatgtgtgtgtgeagggeeteetgatggeegeageegtegtegteetgtgaeeegettggag aaagcctggggtgcctaatgagtgagctaactcacattaattgcgttgcgctcactgcctcactgctttccagtcg TCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGT accaltyttatttetgeaggaatteetggaeageteeeagatgateagtaacegtggttgttatttetgtgeeggggeagtggage ctgggtagggggggggctctgcctcagtgctttcagctaaaaatggggtggggaaccccCaggaggcccggggccgcctggaa gtteeettttetetetetgttettgggaagtegattgageaacageaggggggteaggtgaggeteteetteaetaeegatgeaea ccgagtgetGgggggaggtteteteteteteaggeceaaggeceaagggeetaggecetgeetaggteeeggaaetetCaetettgae ctggcaccctgagtggtgcctcacCTTGTACTCACTCCCAGGTCACTGTCCtcgacGCGGCCGCTCGAcgatAAAATAA aagatititatittagictccagaaaaaggggggaatgaaagaccccacctgtaggttiggclaggtttagtaagtaagcca ttttgcaaggcatggaaaaatacataactgagaatagagaagttcagatcaaggtcggaacagatggaacagcaataaa agageccacarcaetcaetcgggggggcgccagtectecgattgaetgaetcgcccgggtacecgtgtatecaataaacet

GCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCC **AGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAAC** Gaaaactcacgttaagggattttggtcatgagattatcaaaaaggatcttcacctagatcctttaaattaaaatgaag GTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTGGTATG gatottcagcatottttactttcaccagcgtttctgggtgagcaaaaacaggaaggcaaaatgccgcaaaaagggaata **TTTGCGCAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCT** CAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCA GCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTACATGATCCCCCCATGTTGTGCAAAAAAAGCGGTTAGCTCCTT **CGGTCCTCCGATCGTTGTCAGAAGTAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTA CTGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGagtactcaaccaagtcattctgagaatagtgtatgcggcga** cogagttgetettgeeeggegteaacaegggataatacegegeeacatageagaaetttaaaagtgeteateattggaaa acgttetteggggegaaaaeteteaaggatettaeegetgttgagateeagttegatgtaaeeeaetegtgeaeeeaaet agggegacacggaaatgttgaatactcatactcttccttttcaatattattgaagcatttatcagggttattgtctcat gacattaacctataaaaataggcgt

FIG._ 13D

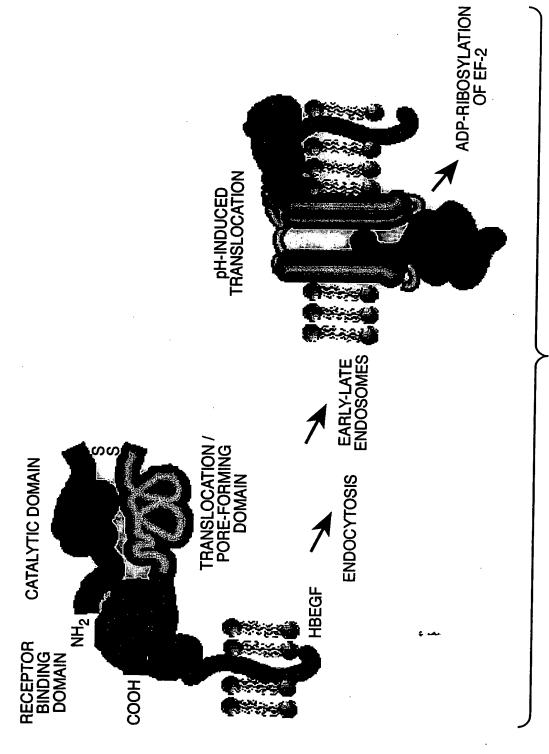
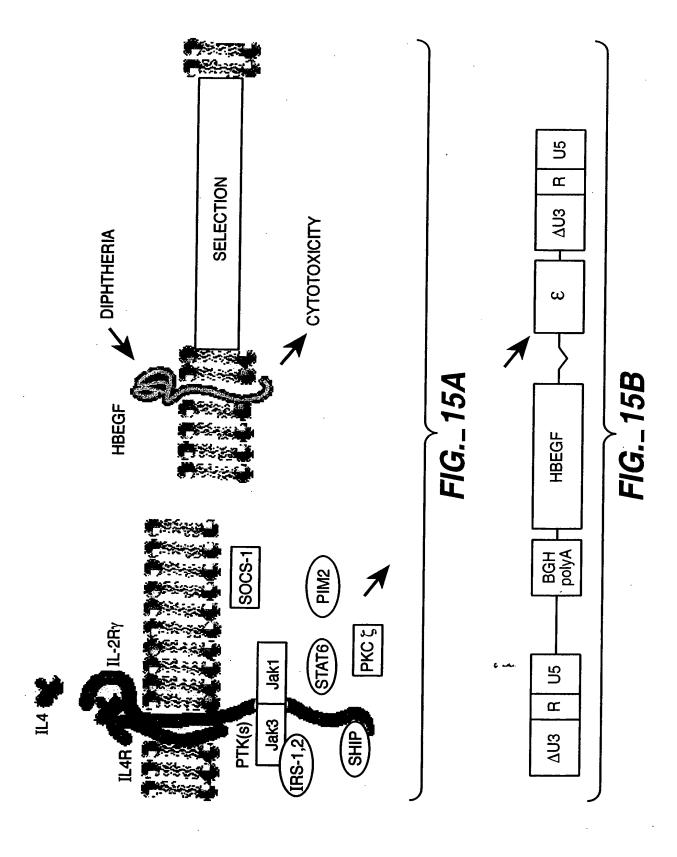


FIG. 14



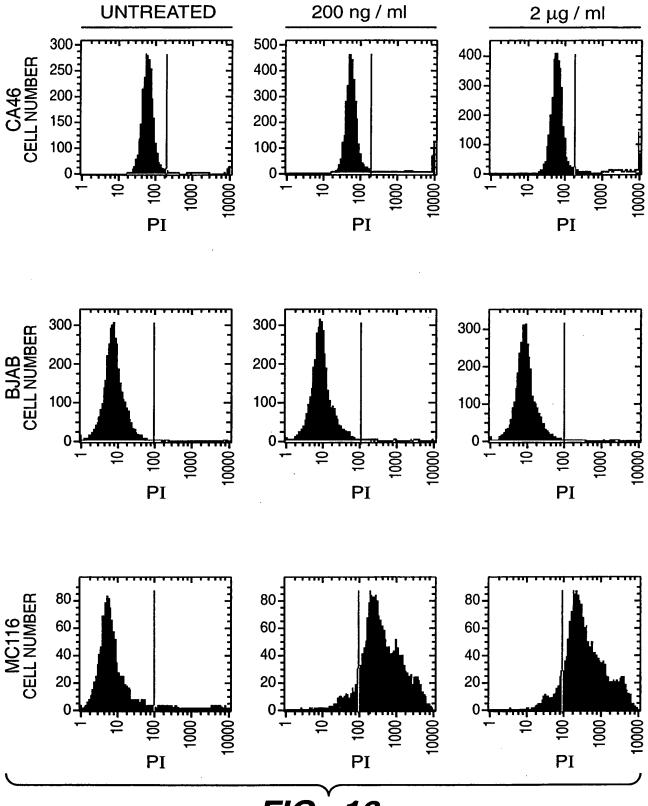


FIG._16

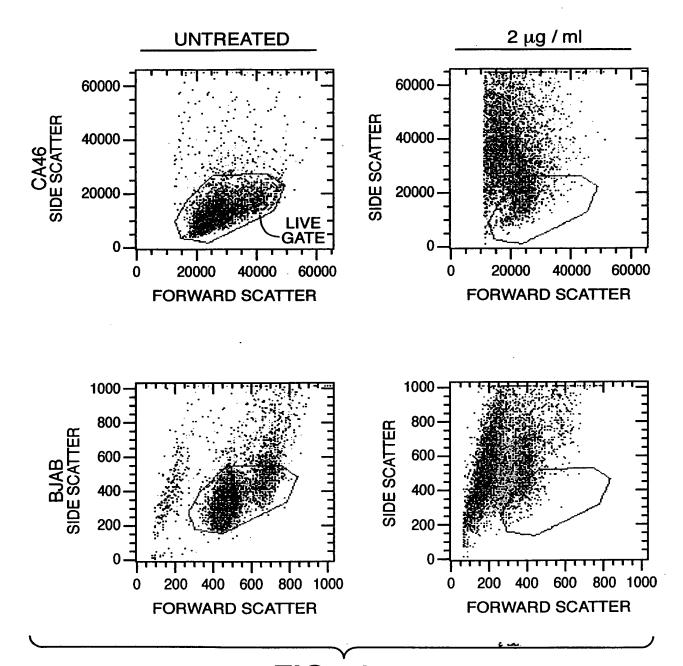
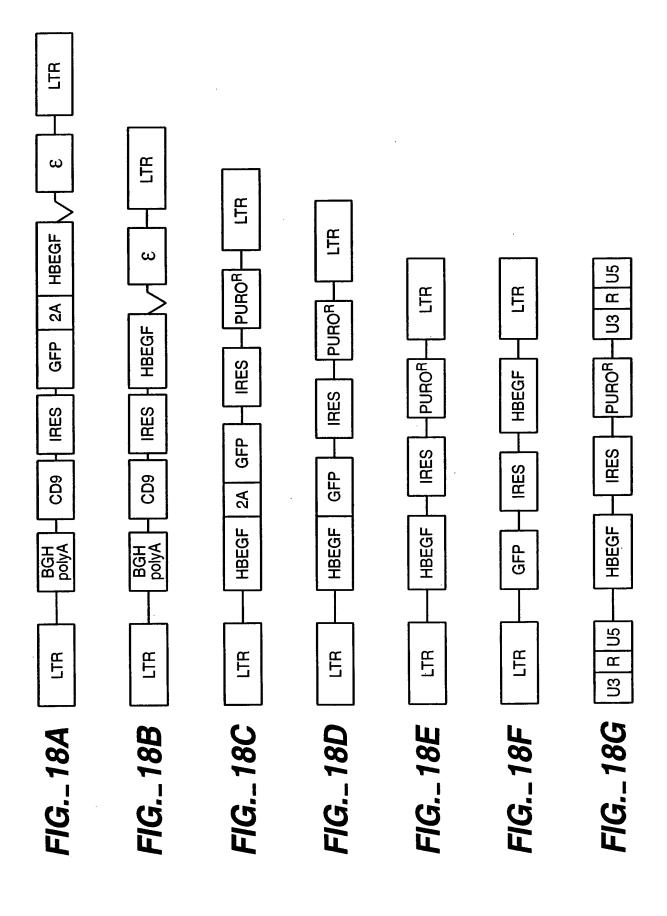


FIG._17



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